

CLAIMS

We claim:

File A3 → 1. A method of inducing an epitope-specific cytotoxic T lymphocyte immune response in a primate comprising the steps of:

(a) delivering into cells of the primate a polynucleotide vaccine, the vaccine comprising both (1) a polynucleotide sequence encoding a viral polyepitope and a major histocompatibility complex class I-restricted peptide epitope and (2) a polynucleotide sequence encoding a hepatitis B core antigen and a major histocompatibility complex class I-restricted peptide epitope, the sequences encoding operably connected to a promoter functional in at least a portion of recipient cells, in an amount sufficient to induce in the primate a cytotoxic T lymphocyte response specific for the major histocompatibility complex class I-restricted peptide epitope; and

(b) following step (a), delivering a live virus vector comprising a polynucleotide coding sequence encoding a viral polyepitope and the major histocompatibility complex class I-restricted peptide epitope of step (a) operably connected to a promoter functional in at least a portion of recipient cells, in an amount sufficient to boost the specific cytotoxic T lymphocyte response induced by the polynucleotide vaccine of step (a).

2. The method of claim 1, wherein the major histocompatibility complex class I-restricted epitope is a viral epitope.

3. The method of claim 1, wherein the primate is a human.

4. The method of claim 2, wherein the viral peptide epitope is a human immunodeficiency virus epitope.

5. The method of claim 2, wherein the viral epitope comprises a portion of the amino acid sequence of a polypeptide selected from the group consisting of human immunodeficiency virus gag, pol, nef, tat, rev, and env.

6. The method of claim 1, wherein step (a) is repeated at least once prior to step (b).

7. The method of claim 1, wherein step (b) is repeated at least once.

8. The method of claim 1, wherein the epitope-specific cytotoxic T lymphocyte response is detectable by tetramer staining of fresh, unstimulated polymorphonuclear blood cells.

9. The method of claim 1, wherein the epitope-specific cytotoxic T lymphocyte response of step (b) is increased relative to the response induced by step (a).

10. The method of claim 2, wherein, subsequent to step (b), the primate is exposed to a virus comprising the viral epitope, and wherein the primate's viral load is lower than the viral load of a comparable naive primate similarly exposed to a virus bearing the viral epitope.

11. The method of claim 1, wherein the vaccine of step (a) is delivered directly into the primate cells by particle bombardment.

12. The method of claim 1, wherein the vaccine of step (a) is delivered into the primate by means of injection.

13. The method of claim 1, wherein after step (b), fresh polymorphonuclear blood cells from the primate produce gamma interferon following exposure to the major histocompatibility complex class I-restricted viral peptide of step (a).

14. The method of claim 1, wherein the major histocompatibility complex class I-restricted epitope is a tumor epitope.

add
As above